

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE  
in its capacity as elected Office

|  |  |
|--|--|
| Date of mailing (day/month/year)<br>19 March 2001 (19.03.01)         |  |
| International application No.<br>PCT/US00/14133                      | Applicant's or agent's file reference<br>07763/044WO1    |
| International filing date (day/month/year)<br>23 May 2000 (23.05.00) | Priority date (day/month/year)<br>24 May 1999 (24.05.99) |
| Applicant<br>TYAGI, Sanjay et al                                     |  |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
21 December 2000 (21.12.00)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

|   |  |
|---|--|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br>Facsimile No.: (41-22) 740.14.35 | Authorized officer<br>Claudio Borton<br>Telephone No.: (41-22) 338.83.38 |
|---|--|

## PATENT COOPERATION TREATY

## PCT

REC'D 22 OCT 2001

WIPO

PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

5

|  |  |  |
|--|--|--|
| Applicant's or agent's file reference<br>07763/044WO1  | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |  |
| International application No.<br>PCT/US00/14133  | International filing date (day/month/year)<br>23 May 2000 (23.05.2000)   | Priority date (day/month/year)<br>24 May 1999 (24.05.1999) |
| International Patent Classification (IPC) or national classification and IPC<br>IPC(7): C12P 19/34; C07H 21/04; A01N 43/04; A61K 31/70 and US Cl. 536/23.1, 24.5; 514/44; 435/91.1, 91.31  |  |  |
| Applicant<br>THE PUBLIC HEALTH RESEARCH INSTITUTE OF THE CITY OF THE CITY OF NEW YORK, INC.  |  |  |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p> <p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input checked="" type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p> |  |  |
| Date of submission of the demand<br>21 December 2000 (21.12.2000)  | Date of completion of this report<br>24 August 2001 (24.08.2001)   |  |
| Name and mailing address of the IPEA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231<br>Facsimile No. (703)305-3230  | Authorized officer<br><i>Janet L. Epps</i><br>Telephone No. 703-308-0196   |  |

Form PCT/IPEA/409 (cover sheet)(July 1998)

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/14133

**I. Basis of the report**

## 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed.
- ☒ the description:  
pages 1-6 \_\_\_\_\_ as originally filed  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☒ the claims:  
pages 7 \_\_\_\_\_, as originally filed  
pages NONE \_\_\_\_\_, as amended (together with any statement) under Article 19  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☒ the drawings:  
pages NONE \_\_\_\_\_, as originally filed  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☒ the sequence listing part of the description:  
pages NONE \_\_\_\_\_, as originally filed  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/14133

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

|                               |                    |     |
|-------------------------------|--------------------|-----|
| Novelty (N)                   | Claims <u>NONE</u> | YES |
|                               | Claims <u>1-4</u>  | NO  |
| Inventive Step (IS)           | Claims <u>NONE</u> | YES |
|                               | Claims <u>1-4</u>  | NO  |
| Industrial Applicability (IA) | Claims <u>1-4</u>  | YES |
|                               | Claims <u>NONE</u> | NO  |

**2. CITATIONS AND EXPLANATIONS (Rule 70.7)**

Claims 1-4 lack novelty under PCT Article 33(2) as being anticipated by Kool.

Claims 1-4 read on an antisense oligonucleotide consisting of a central loop sequence that is complementary to a selected messenger RNA target sequence and that is flanked by 3' and 5' arm sequences that are complementary to one another.

Kool et al. disclose oligonucleotides which form a stem-loop structure for a time under conditions sufficient to The present invention is directed to stem-loop oligonucleotides including a double-stranded stem domain of at least about 2 base pairs and a single-stranded loop domain. The loop domain has at least one parallel binding (P) domain that is separated by at least about 3 nucleotides from a corresponding anti-parallel binding (AP) domain. According to the present invention each P and corresponding AP domain can simultaneously and detectably bind to one strand of a defined nucleic acid target. However, the P domain binds in a parallel manner to the target while the corresponding AP domain binds in an anti-parallel manner to the target. In one embodiment the target has a known nucleotide sequence from which at least 5 nucleotide positions in the P domain and in the corresponding AP domain are determined according to the rules provided by the present invention. Moreover the two strands of the stem can be covalently cross-linked. The present stem-loop oligonucleotides can be expressed within or taken up by a cell (col. 3, lines 29-46).

Claims 1-4 lack an inventive step under PCT Article 33(3) as being obvious over Kool for the reasons set forth above.

----- NEW CITATIONS -----

NONE

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

International application No.

PCT/US00/14133

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

Claim 1 is objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: Claim 1 recites the term "flankded", this term is incorrectly spelled, the appropriate term is likely "flanked."

# PATENT COOPERATION TREATY

WJH

From the INTERNATIONAL SEARCHING AUTHORITY

|   |
|---|
| To: WILLIAM J. HONE<br>FISH & RICHARDSON P.C.<br>45 ROCKEFELLER PLAZA<br>SUITE 2800<br>NEW YORK, NY 10111 |
|---|

**RECEIVED**  
 AUG 22 2000  
 FISH & RICHARDSON, P.C.  
 NEW YORK CITY OFFICE

## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

|   |   |
|---|---|
| Applicant's or agent's file reference<br>07763/044WO1                           | Date of Mailing (day/month/year) <b>18 AUG 2000</b>       |
| International application No.<br>PCT/US00/14133                                 | International filing date (day/month/year)<br>23 MAY 2000 |
| Applicant<br>THE PUBLIC HEALTH RESEARCH INSTITUTE OF THE CITY OF NEW YORK, INC. |   |

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.  
**Filing of amendments and statement under Article 19:**  
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46).  
**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.  
**Where?** Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35  
*Search Report - Rspn 18-18-00*  
*Confirm PCT Abstract 9-18-00*  
 For more detailed instructions, see the notes on the accompanying sheet.
2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
  - ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
  - ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4. Further action(s): The applicant is reminded of the following:
  - Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.
  - Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).
  - Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

|   |   |
|---|---|
| Name and mailing address of the ISA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231<br>Facsimile No. (703) 305-3230 | Authorized officer<br>JANET LEE EPPS<br><i>Durthea Lawrence</i><br>Telephone No. (703) 308-0196 |
|---|---|

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: WILLIAM J. HONE  
FISH & RICHARDSON P.C.  
45 ROCKEFELLER PLAZA  
SUITE 2800  
NEW YORK, NY 10111

## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Date of Mailing  
(day/month/year)

18 AUG 2000

Applicant's or agent's file reference  
07763/044WO1

**FOR FURTHER ACTION** See paragraphs 1 and 4 below

International application No.  
PCT/US00/14133

International filing date  
(day/month/year)  
23 MAY 2000

Applicant  
THE PUBLIC HEALTH RESEARCH INSTITUTE OF THE CITY OF NEW YORK, INC.

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.  
☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 *bis* 1 and 90 *bis* 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

JANET LEE EPPS

Telephone No. (703) 308-0196

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|   |  |   |
|---|--|---|
| Applicant's or agent's file reference<br>07763/044WO1                           | <b>FOR FURTHER ACTION</b>  | see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. |
| International application No.<br>PCT/US00/14133                                 | International filing date ( <i>day/month/year</i> )<br>23 MAY 2000 | (Earliest) Priority Date ( <i>day/month/year</i> )<br>24 MAY 1999   |
| Applicant<br>THE PUBLIC HEALTH RESEARCH INSTITUTE OF THE CITY OF NEW YORK, INC. |  |   |

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
2. ☐ Certain claims were found unsearchable (See Box I).
3. ☐ Unity of invention is lacking (See Box II).
4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:
5. With regard to the abstract,

☐ the text is approved as submitted by the applicant.

☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/14133

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12P 19/34; C07H 21/04; A01N 43/04; A61K 31/70

US CL : 536/23.1, 24.5; 514/44; 453/91.1, 91.31

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1, 24.5; 514/44; 453/91.1, 91.31

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS, MEDLINE, BIOSIS, USPAT, EPO, JPO, DERWENT

search terms: (hairpin or stem loop or central loop) and (antisense or oligonucleotide)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|-----------|--|-----------------------|
| X         | US 5,514,546 A (KOOL) 07 May 1996, see figure 1.   | 1-4                   |
| A         | JENDIS et al. Inhibition of Replication of Fresh HIV Type 1 Patient Isolates by a Polypurine Tract-Specific Self-Complementary Oligodeoxynucleotide. Aids Research and Human Retroviruses. 1996, Vol. 12, No. 12, pages 1161-1168, especially page 1167. | 1-4                   |



Further documents are listed in the continuation of Box C.



See patent family annex.

|   |  |
|---|--|
| * Special categories of cited documents:  | *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| *A* document defining the general state of the art which is not considered to be of particular relevance  | *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| *E* earlier document published on or after the international filing date  | *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | *G* document member of the same patent family  |
| *O* document referring to an oral disclosure, use, exhibition or other means  |  |
| *P* document published prior to the international filing date but later than the priority date claimed  |  |

Date of the actual completion of the international search

12 JULY 2000

Date of mailing of the international search report

18 AUG 2000

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

JANET LEE EPPS

Telephone No. (703) 308-0196

**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US00/14133

**Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)**

This invention relates to hairpin antisense oligonucleotides and their therapeutic use.

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty and of the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

**What parts of the international application may be amended ?**

The claims only.

The description and the drawings may only be amended during international preliminary examination under Chapter II.

**When ?** Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

**Where not to file the amendments ?**

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been filed, see below.

**How ?** Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

**What documents must/may accompany the amendments ?**

**Letter (Section 205(b)):**

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confounded with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

## NOTES TO FORM PCT/ISA/220 (continued)

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under Article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

The statement should be brief, it should not exceed 500 words if in English or if translated into English.

It should not be confounded with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It should not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### In what language ?

The amendments must be made in the language in which the international application is published. The letter and any statement accompanying the amendments must be in the same language as the international application if that language is English or French; otherwise, it must be in English or French, at the choice of the applicant.

### Consequence if a demand for international preliminary examination has already been filed ?

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase ?

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/14133**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : C12P 19/34; C07H 21/04; A01N 43/04; A61K 31/70

US CL : 536/23.1, 24.5; 514/44; 453/91.1, 91.31

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1, 24.5; 514/44; 453/91.1, 91.31

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAPLUS, MEDLINE, BIOSIS, USPAT, EPO, JPO, DERWENT

search terms: (hairpin or stem loop or central loop) and (antisense or oligonucleotide)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|-----------|--|-----------------------|
| X         | US 5,514,546 A (KOOL) 07 May 1996, see figure 1.   | 1-4                   |
| A         | JENDIS et al. Inhibition of Replication of Fresh HIV Type 1 Patient Isolates by a Polypurine Tract-Specific Self-Complementary Oligodeoxynucleotide. Aids Research and Human Retroviruses. 1996, Vol. 12, No. 12, pages 1161-1168, especially page 1167. | 1-4                   |

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

|   |  |
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Date of the actual completion of the international search

12 JULY 2000

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18 AUG 2000

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